AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-11 (Canceled)

12(Previously Presented): A high-throughput method for assaying for changes in protein-protein interactions in response to a test agent comprising:

(a) introducing one or more prey proteins in cells,

wherein the prey proteins are labeled with an epitope tag permitting separation of the prey proteins from other proteins in the cells and

wherein the prey proteins can interact with a SMURF to form protein-protein interactions which define a network of interactions involved in signal transduction pathways regulated by a SMURF;

(b) introducing one or more bait protein in the cells, wherein the bait protein is a SMURF labeled with a detectable substance permitting identification of the bait protein and protein-protein interactions comprising a prey protein and the bait protein;

(c) inducing formation of the protein-protein interactions in the presence of the test agent;

(d) assaying in a high-throughput format the protein-protein interactions; and

(e) comparing the assayed protein-protein interactions with protein-protein interactions assayed in the absence of the test agent.

13(Canceled).

14(Previously Presented): A method of claim 12 wherein an increase in the protein-protein interactions with a test agent indicates that the agent is an agonist of the interaction and a decrease in the amount of protein-protein interactions indicates that the agent is an antagonist.

15(Previously Presented): A method of claim 12 wherein the cells are mammalian cells.

16-18(Canceled).

19(Previously Presented): A method as claimed in claim 12 wherein the detectable substance is an enzyme, radioisotope, fluorescent label, luminescent label, or an enzymatic label.

20(Previously Presented): A method of claim 19 wherein the detectable substance is an enzymatic label.

21(Previously Presented): A method of claim 20 wherein the detectable substance is luciferase.

22(Previously Presented): A method as claimed in claim 12 wherein two or more prey proteins are introduced into the cells.

23(Previously Presented): A method of claim 12 wherein the epitope tag is FLAG, hemagglutinin, His6 or an Ig sequence.

24(Canceled).

25(Previously Presented): A method of claim 12 wherein the prey protein comprises a library of protein sequences.

26-31(Canceled).

32(Currently Amended): A method of claim 12 wherein in step (e) the protein-protein interactions are compared using a ~~matix~~ matrix comprising a color gradient displaying the magnitude of the protein–protein interactions.

33(Previously Presented): A method of claim 32 wherein the matrix comprises 100 by 100 protein-protein interactions.

34-35(Canceled).

36(Previously Presented): A method of claim 12 wherein steps (a) to (e) are performed using an integrated modular system.

37(Previously Presented): A method of claim 12 wherein step (d) further comprises purifying proteins of the protein-protein interactions in an automated immunoprecipitation module, preparing fragments of the proteins suitable for mass spectrometry in an analysis module; and analyzing the fragments in a mass spectrometer module.

38(New). A high-throughput method for assaying for changes in protein-protein interactions in response to a test agent comprising:

(A) introducing into a cell culture

i. mammalian cells expressing

(a) one or more prey proteins, at least one prey protein labeled with FLAG, wherein the prey proteins interact with a SMURF to form protein-protein interaction complexes involved in a TGFβ signaling pathway regulated by a SMURF; and

(b) one or more SMURF proteins labeled with an enzymatic label; and

ii. a test agent;

(B) inducing TGF-β signaling in the mammalian cells to form protein-protein interaction complexes between the prey proteins and SMURF:

(C) isolating the protein-protein interaction complexes that bind to an antibody to FLAG;

(D) introducing into the isolated protein-protein interaction complexes a substrate for the enzymatic label, wherein a level of detectable signal generated by the enzymatic label and its substrate indicates the level of the protein: protein interaction complexes; and

(E) comparing the level of the interaction complexes of step (D) with a level of interaction complexes that form in the absence of the test agent, or a level of interaction complexes that form in the absence of step (B).

39(New). A method of claim 38 wherein an increase in the level of protein-protein interaction complexes with a test agent indicates that the agent is an agonist of the interaction and a decrease in the amount of protein-protein interaction complexes indicates that the test agent is an antagonist.

40(New): A method of claim 38 wherein the enzymatic label is luciferase.

41(New): A method of claim 38 wherein the prey proteins comprise a library of protein sequences.

42(New): A method of claim 38 wherein in step (E) the protein-protein interactions are compared using a matrix comprising a color gradient displaying the magnitude of the protein–protein interactions.

43(New): A method of claim 38 wherein steps (A) to (E) are performed using an integrated modular system.

44(New): A method of claim 38 further comprising purifying proteins of the protein-protein interactions in an automated immunoprecipitation module, preparing

fragments of the proteins suitable for mass spectrometry in an analysis module; and analyzing the fragments in a mass spectrometer module.